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| APPLICATION NO.               | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.    | CONFIRMATION NO. |
|-------------------------------|-------------|----------------------|------------------------|------------------|
| 10/552,000                    | 10/04/2005  | Hiroko Yanaga        | 1752-0173PUS1          | 6374             |
| 2292                          | 7590        | 11/05/2007           | EXAMINER               |                  |
| BIRCH STEWART KOLASCH & BIRCH |             |                      | GOUGH, TIFFANY MAUREEN |                  |
| PO BOX 747                    |             |                      | ART UNIT               | PAPER NUMBER     |
| FALLS CHURCH, VA 22040-0747   |             |                      | 1657                   |                  |
| NOTIFICATION DATE             |             | DELIVERY MODE        |                        |                  |
| 11/05/2007                    |             | ELECTRONIC           |                        |                  |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

|                              |                  |                |
|------------------------------|------------------|----------------|
| <b>Office Action Summary</b> | Application No.  | Applicant(s)   |
|                              | 10/552,000       | YANAGI, HIROKO |
|                              | Examiner         | Art Unit       |
|                              | Tiffany M. Gough | 1657           |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 20 August 2007.  
 2a) This action is FINAL.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-4 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-4 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

|  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____. _____   | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/20/2007 has been entered.

### ***Claim Objections***

Claim 1 is objected to because of the following informalities: Applicant claims a method of producing human chondrocytes, however applicants method comprises co-culturing chondrocytes..., not specifically requiring the chondrocytes to be human. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The 112 first paragraph rejection of record has been withdrawn due to applicant's amendment.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 stand rejected under 35 U.S.C. 102(b) as being anticipated by Klein-Nulend et al (Tissue Engineering, vol 4, 1998).

Applicant claims a method of producing human chondrocytes by co-culturing chondrocytes together with the perichondrium, wherein no exogenous feeder cells are present in culture. The cartilage tissue from which the chondrocytes are isolated from is preferably auricular cartilage.

Klein-Nulend teach culturing human auricular perichondrium containing chondrocytes, wherein no exogenous feeder cells are present in culture (see Materials and Methods section,p.306 and Results section, p.308-310).

Thus, the reference anticipates the claimed subject matter.

Applicant argues that Klein-Nulend disclose differentiation of progenitor cells and that the method of Klein-Nulend does not disclose culturing with chondrocytes. The perichondrium from ear or rib is disclosed as a convenient source of cells with chondrogenic potential, i.e. chondrocytes and it is further disclosed that perichondrium cells when transplanted provide a practical source of autologous cells with

chondrogenic potential. Although chondrocytes are not literally disclosed, progenitor cells with chondrogenic potential from human perichondrium are disclosed. Further, it is known in the art that chondrogenic progenitor cells differentiate into chondrocytes under appropriate conditions. Further, applicants process recites the language comprises, thus, not limiting their method to the claimed steps.

Claims 1-4 stand rejected under 35 U.S.C. 102(b) as being anticipated by Van Osch et al (Plastic and Reconstructive Surgery, 2001).

Applicant claims a method of producing human chondrocytes by co-culturing chondrocytes together with the pericondrium, wherein no exogenous feeder cells are present in culture. The culture is seeded to form a monolayer to give a chondrocyte mass. The cartilage tissue from which the chondrocytes are isolated from is preferably auricular cartilage.

Van Osch teach isolating human auricular cartilage and culturing the isolated chondrocytes in a monolayer for 3-4 passages (see Materials and Methods section, p. 434). The human cells were also seeded into alginate (see Results section, p. 435). No exogenous feeder cells are present in culture.

Although the reference does not necessarily teach the chondrocytes to be co-cultured with the pericondrium, human auricular cartilage is known to be coated with pericondrium, thus the chondrocytes isolated by the disclosed method must essentially be coated with the perichondrium and therefore co-cultured together with the perichondrium of the cartilage from which it was isolated.

Therefore, the reference anticipates the claimed subject matter.

Applicant's arguments have been considered but are not persuasive because applicants argue limitations not in the claims; thus, the arguments are not commensurate in scope with the claims. Applicant first argues that their method is a different process because the culture medium is centrifuged, not filtered. Such limitation is not claimed in applicant's process. Secondly, applicant argues the difference in multiplication, stating that the cell count of their invention increased about 1000 times compared to the cell count of the subculture. Such limitation is not claimed in applicant's process. Thirdly, applicant argues the difference of production of Collagen type II marker. Such step is not claimed in the instant application. Thus, applicant's arguments are not commensurate in scope with the claimed invention.

Claim 1 stands rejected under 35 U.S.C. 102(b) as being anticipated by Larson et al (Matrix Biology, 2002).

Applicant claims a method of producing human chondrocytes by co-culturing chondrocytes together with the pericordium, wherein no exogenous feeder cells are present in culture.

Larson et al teach producing human chondrocytes by co-culturing chondrocytes with their pericellular matrix attached and no exogenous feeder cells were added to the culture.

Thus, the reference anticipates the claimed subject matter.

Applicant argues that Larson discloses articular cartilage and that articular cartilage does not have perichondrium, the examiner is directed to Exhibit A. Exhibit A is not in English, therefore the teachings of Exhibit A cannot be found. Applicant also directs the examiner to Exhibit B, however as stated in the Advisory action 6/29/2007, Exhibit B has not been received nor has it been entered into the case. Therefore, Exhibits A and B have not been considered. Applicant also states in both priority documents paragraphs (0017) that the "...chondrocytes of any human cartilage having perichondrium bonded thereto such as auricular...articular cartilage...." Thus, applicant themselves teach articular cartilage to have perichondrium. Also, see Long et al (Ref. CB on IDS filed 6/27/2006). Applicants arguments are contradictory and are not persuasive.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Van Osch et al (Tissue Engineering, 2000).

Applicant claims a method of producing human chondrocytes by co-culturing chondrocytes together with the perichondrium, wherein no exogenous feeder cells are present in culture. The culture is seeded to form a monolayer to give a chondrocyte mass. The cartilage tissue from which the chondrocytes are isolated from is preferably auricular cartilage.

Van Osch et al teach perichondrium to be a new "young" autologous cartilage suitable for nasal septum perforation in a child. They teach growing cartilage in vitro from auricular perichondrium (p.322). The perichondrium is known to possess the

chondrocytes and also the ability to generate cartilage (see p.325,328). The perichondrium explants were cultured and grown to form a monolayer (p.322-325). Thus, given that the perichondrium is known to contain chondroprogenitor cells, Van Osch teaches co-culturing from a cartilage having chondrocytes and perichondrium.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Long et al (Development,1998).

Applicant claims a method of producing human chondrocytes by co-culturing chondrocytes together with the pericordium, wherein no exogenous feeder cells are present in culture.

Long et al teach co-culturing chondrocytes together with the perichondrium (see p.1070 Local effects of perichondrium section continued to 1071).

Thus, the reference anticipates the claimed subject matter.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hiroko et al (WO 02/012451 A1, see English language equivalent Hiroko et al, EP1331264A1) in view of Van Osch et al (Tissue Engineering, 2000) or Klein-Nulend et

al (Tissue Engineering, vol 4, 1998) supported by Yi et al (Abstract, J. Korean Soc. Plastic Reconst. Surg., 2001).

Applicant claims a method of producing human chondrocytes, preferably auricular chondrocytes, from cartilage together with the perichondrium comprising growing cells either as a monolayer or multilayer seeding to give a chondrocyte mass.

Hiroko et al (WO 02/012451 A1, see equivalent EP1331264A1) disclose a method of co-culturing human chondrocytes together with perichondrial cells to produce large amounts of human chondrocytes in culture and further multilayer seeding to give to obtain a chondrocyte mass. Hiroko teaches utilization of a cartilage matrix containing collagen and a cartilage therapy material incorporating their chondrocyte mass. The human chondrocytes used in the invention may be any cartilage tissue such as auricular, costal, articular, intervertebral, or tracheal cartilage, especially auricular, costal and articular cartilage (see EP1331246A1 p.3 lines 18-20). Although Hiroko teach the use of feeder cells, specifically non-human animal cells, they do disclose that the feeder cells used contribute to the proliferation and differentiation of the chondrocytes to maintain characteristics of the original cartilage tissue (0017 and 0018). They further teach that no feeder cells have been known for human chondrocytes.

As stated above, Van Osch et al teach perichondrium to be a new "young" autologous cartilage suitable for nasal septum perforation in a child. They teach growing cartilage in vitro from auricular perichondrium (p.322). The perichondrium is known to possess the chondrocytes and also the ability to generate cartilage (see p.325,328). Klein-Nulend also teach that the perichondrium from ear or rib is disclosed

as a convenient source of cells with chondrogenic potential, i.e. chondrocytes and it is further disclosed that perichondrium cells when transplanted provide a practical source of autologous cells with chondrogenic potential.

Yi et al teach that the perichondrium is a new source of cartilage for auricular cartilage grafts. They teach grafts wherein the perichondrium is preserved and further suggest the perichondrium to produce chondrogenic cells and serves as a scaffold for cartilage differentiation.

At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to have co-cultured chondrocytes together with the perichondrium because while Hiroko disclose that the feeder cells used contribute to the proliferation and differentiation of the chondrocytes to maintain characteristics of the original cartilage tissue (0017 and 0018), they further teach that no feeder cells have been known for human chondrocytes. Thus, there is a need for “feeder cells” for human chondrocytes. Therefore, given what is known in the art of the proliferative and differentiation abilities of the perichondrium, its ability to generate and maintain characteristics of cartilage, and it's chondrogenic potential as taught by Van Osch and Klein-Nulend further supported by Yi et al, one would have been motivated to co-culture chondrocytes with it's perichondrium intact.

Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to have co-cultured chondrocytes with its perichondrium with a reasonable expectation for successfully producing human chondrocytes because there is a need in the art for cells/tissues which are capable of supporting the

proliferation and differentiation of chondrocytes. Given the ability of the perichondrium to do so as is taught by Van Osch and Klein-Nulend further supported by Yi et al, one would have expected success in co-culturing chondrocytes with its intact perichondrium.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tiffany M. Gough whose telephone number is 571-272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tiffany Gough  
/Ruth A Davis/  
Primary Examiner, AU 1651